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This listing of claims will replace all prior versions, and listings, of claims in the application.

## **Listing of Claims:**

Claims 1-6 (Withdrawn from consideration).

- 7. (Canceled)
- 8. (Currently Amended) The compound of claim [[101]] 112 wherein said amino acid is amino caproic acid.
- 9. (Currently Amended) The compound of claim [[101]]  $\underline{112}$  wherein said  $X_4$  is the side chain of glutamic acid.
- 10. (Currently Amended) The compound of claim [[101]]  $\underline{112}$  wherein said  $X_6$  has one of the formulas:

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## wherein:

SS is a solid support;  $X_7$  is O or CH<sub>2</sub>; Bx is a nucleobase, C<sub>4</sub>-C<sub>14</sub> heterocyclyl or hydrogen; z is an integer from 1 to 50; and u is an integer from 2 to 5.

11. (Currently Amended) The compound of claim [[101]]  $\underline{112}$  wherein said  $R_1$  is dimethoxytrityl.

12. (Canceled)

Claims 13-20 (Withdrawn from consideration)

Claims 21-31 (Canceled)

32. (Previously Presented) The method of claim 104 wherein  $W_1$  has the formula  $-O-(CH_2)_n$ -NH-, wherein n is from 1 to about 10.

33. (Original) The method of claim 32 wherein n is 6.

34. (Canceled)

35. (Previously Presented) The method of claim 104 wherein  $R_1$  is dimethoxytrityl, A has the formula -O-( $CH_2$ )<sub>n</sub>-NH- where n is 6, m is 2,  $R_4$  is t-butoxy,  $R_5$  is trifluoroacetoyl,  $R_6$  is -C(=O)- $CH(CH_3)_2$ , and  $R_{30}$  is FMOX.

Claims 36-39 (Canceled).

40. (Previously Presented) The method of claim 105 wherein  $R_1$  is dimethoxytrityl,  $W_1$  has the formula -O-(CH<sub>2</sub>)<sub>n</sub>-NH- where n is 6, m is 2,  $R_4$  is t-butoxy,  $R_5$  is trifluoroacetoyl,  $R_6$  is -C(=O)-CH(CH<sub>3</sub>)<sub>2</sub>, and  $R_{30}$  is FMOX.

41. (Canceled)

42. (Previously Presented) The method of claim 26 wherein said compound IX is prepared by reacting folic acid:

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with a reagent effective to form pterin aldehyde:

$$\begin{array}{c|c} O & O \\ \hline \\ N & NH \\ \hline \\ N & NH_2 \\ \end{array}$$

and

protecting the amino group of said pterin aldehyde.

Claims 43 and 44 (Withdrawn from consideration).

Claims 45-62 (Canceled).

63 (Previously Presented). The compound of claim [[107]] 115 wherein m is 2.

64. (Original) The compound of claim 63 wherein  $W_1$  is  $-O-(CH_2)_6$ -NH-.

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65. (Previously Presented) The compound of claim 64 wherein  $R_4$  is t-butoxy.

66 (Original). The compound of claim 65 wherein R<sub>1</sub> is dimethoxytrityl, R<sub>5</sub> is trifluoroacetoyl, and R<sub>6</sub> is

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 $-C(=O)-CH(CH_3)_2$ .

67 (Original). The compound of claim 66 wherein q is 0.

Claims 68-71 (Canceled).

72 (Original). A composition comprising a compound of claim 63, said composition being substantially free of a compound of formula XVA, XVB, XVC or XVD:

XVD

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$$R_{1} = 0$$

$$R_{21}$$

$$R_{21}$$

$$R_{20}$$

$$R_{15}$$

$$R_{20}$$

$$R_{15}$$

$$R_{1} = 0$$

$$R_{21}$$

$$R_{1} = 0$$

$$R_{1} = 0$$

$$R_{1} = 0$$

$$R_{21}$$

$$R_{1} = 0$$

$$R_{1} = 0$$

$$R_{20}$$

$$R_{21}$$

$$R_{20}$$

$$R_{21}$$

$$R_{20}$$

$$R_{21}$$

$$R_{20}$$

$$R_{21}$$

wherein  $W_{15}$  has the formula:

$$\left\{ -W_1 - C - (CH_2)_2 - CH - NH \right\}$$

$$R_4 O$$

$$R_5 N N NH$$

$$R_6 C + CH_2 + CH_2 + CH_2 + CH_3 + CH_4 + CH_4 + CH_5 + CH_$$

XVC

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Claims 73-78 (Canceled).

79 (Previously Presented). The compound of claim [[108]] 116 wherein m is 2.

80 (Original). The compound of claim 79 wherein  $W_1$  is -O-( $CH_2$ )<sub>n</sub>-NH- wherein n is from 1 to about 10.

81 (Original). The compound of claim 80 wherein n is 6.

Claims 82-87 (Canceled).

88. (Previously Presented) The compound of claim [[109]] 117 wherein m is 2.

89. (Original) The compound of claim 88 wherein  $W_1$  is -O-(CH<sub>2</sub>)<sub>n</sub>-NH- wherein n is from 1 to about 10.

90. (Original) The compound of claim 89 wherein n is 6.

Claims 91 and 92 (Withdrawn from consideration).

93 (Currently Amended). The compound of claim [[101]]  $\underline{112}$  wherein said  $R_4$  is a hydroxyl group protected with  $C_1$ - $C_{10}$  alkyl,  $C_2$ - $C_{10}$  alkenyl or  $C_2$ - $C_{20}$  alkynyl.

Claims 94-100 (Withdrawn from consideration).

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Claims 101-103 (Canceled).

104 (Currently Amended) A synthetic method comprising the steps of:

(a) providing a compound of formula IA, IB, IC or ID:

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 $\dot{R}_{20}$ 

IC

 $\dot{R}_{21}$ 

$$R_1$$
—O  $B$ 
 $W_{1a}$   $R_{21}$ 
 $W_{1a}$   $R_{21}$ 
 $W_{1a}$   $R_{21}$ 
 $W_{1a}$   $Q$ 
 $W_{1a}$   $Q$ 

ID

wherein:

 $W_{1a}$  is  $W_{1b}\text{-H},\,\text{OH},\,\text{NH}_2$  or SH, where  $W_{1b}$  is a linking group;

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R<sub>1</sub> is H or a hydroxyl protecting group;

B is a nucleobase;

each R<sub>21</sub> is H, OH, F, or a group of formula Z-R<sub>22</sub>-(R<sub>23</sub>)<sub>v</sub>;

Z is O, S, NH, or N- $R_{22}$ - $(R_{23})_v$ 

 $R_{22}$  is  $C_1$ - $C_{20}$  alkyl,  $C_2$ - $C_{20}$  alkenyl, or  $C_2$ - $C_{20}$  alkynyl;

R<sub>23</sub> is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether, a group that enhances the pharmacodynamic properties of oligonucleotides, or a group that enhances the pharmacokinetic properties of oligonucleotides;

v is from 0 to about 10;

or  $R_{21}$  has one of the formulas:

$$-(O)_{y1}-(CH_2)_{y2}$$
  $O-E$ 

$$--(O)_{y1} - (CH_2)_{y2} - O - N - (CH_2)_{y2} - O - E$$

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wherein:

y1 is 0 or 1;

y2 is 0 to 10;

y3 is 1 to 10;

E is  $N(R_{41})(R_{42})$  or  $N=C(R_{41})(R_{42})$ ;

each  $R_{41}$  and each  $R_{42}$  is independently H,  $C_1$ - $C_{10}$  alkyl, a nitrogen protecting group, or  $R_{41}$  and  $R_{42}$  taken together form a nitrogen protecting group; or  $R_{41}$  and  $R_{42}$  taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

q is from zero to about 50, provided that when said compound has formula ID, q is at least 1;

M is an optionally protected internucleoside linkage;

(b) reacting said compound of formula I with a compound of formula II:

$$R_{30}$$
—NH $-X_3$ -C-OH

Π

wherein:

 $R_{30}$  is an amino protecting group;

 $X_3$  is a group of formula XII:

$$\{$$
  $\}_{m}$ 

XII

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wherein m is 1 or 2;

 $R_4$  is a hydroxyl group, or a protected hydroxyl group; to form a compound of formula IVA, IVB, IVC, or IVD:

$$R_1$$
-O  $B$ 
 $R_{21}$ 
 $q$ 
 $R_{20}$ 
 $M$ 
 $R_{20}$ 
 $M$ 
 $R_{20}$ 
 $M$ 

$$W_{4} = \begin{bmatrix} 0 & B \\ R_{21} & q \\ R_{20} & R_{21} \end{bmatrix}$$

$$IVC$$

wherein:

W<sub>4</sub> has the formula:

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where  $W_1$  is a linking group, O, NH, or S; and treating said compound of formula IVA, IVB, IVC or IVD with a deprotecting reagent to form a compound of formula VA, VB, VC or VD:

wherein W<sub>5</sub> has the formula:

$$\left\{ \begin{matrix} O \\ - W_1 \end{matrix} \begin{matrix} \begin{matrix} O \\ \parallel \end{matrix} \begin{matrix} - C \end{matrix} - X_3 - NH_2 \end{matrix} \right\}$$
 and

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(c) condensing said compound of Formula V with a compound of Formula VI:

$$O \longrightarrow N \longrightarrow NH$$

$$R_5 \longrightarrow N \longrightarrow NH$$

$$R_6$$

VI

wherein:

R<sub>5</sub> is H or an amino protecting group;

R<sub>6</sub> is H or an amino protecting group;

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to form a compound of Formula VIIA, VIIB, VIIC, or VIID:

$$\begin{array}{c|c} W_7 & & & \\ \hline \\ M & & \\ \hline \\ R_{20} & R_{21} \end{array} \qquad \begin{array}{c} q \\ \\ R_{20} & R_{21} \end{array}$$

VIIC

VIID

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wherein  $W_7$  has the Formula:

$$\{-w_1-C-x_3-NH \} \\ 0 \\ R_5 \\ N \\ NH \\ R_6 \\ R_$$

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## 105. (Currently Amended) A synthetic method comprising the steps of:

(a) providing a compound of formula IA, IB, IC or ID:

$$R_1$$
— $O$ 
 $M$ 
 $W_1a$ 
 $Q$ 
 $R_{20}$ 
 $R_{21}$ 

ID

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wherein:

W<sub>1a</sub> is W<sub>1b</sub>-H, OH, NH<sub>2</sub> or SH, where W<sub>1b</sub> is a linking group;

R<sub>1</sub> is H or a hydroxyl protecting group;

B is a nucleobase;

each R<sub>21</sub> is H, OH, F, or a group of formula Z-R<sub>22</sub>-(R<sub>23</sub>)<sub>v</sub>;

Z is O, S, NH, or N- $R_{22}$ - $(R_{23})_{\nu}$ 

 $R_{22}$  is  $C_1$ - $C_{20}$  alkyl,  $C_2$ - $C_{20}$  alkenyl, or  $C_2$ - $C_{20}$  alkynyl;

R<sub>23</sub> is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether, a group that enhances the pharmacodynamic properties of oligonucleotides, or a group that enhances the pharmacokinetic properties of oligonucleotides;

v is from 0 to about 10;

or  $R_{21}$  has one of the formulas:

$$(O)_{y1}$$
  $--(CH_2)_{y2}$   $O$   $--E$ 

$$--(O)_{y_1} - (CH_2)_{y_2} - O - N - (CH_2)_{y_2} - O - E$$

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wherein:

y1 is 0 or 1;

y2 is 0 to 10;

y3 is 1 to 10;

E is  $N(R_{41})(R_{42})$  or  $N=C(R_{41})(R_{42})$ ;

each  $R_{41}$  and each  $R_{42}$  is independently H,  $C_1$ - $C_{10}$  alkyl, a nitrogen protecting group, or  $R_{41}$  and  $R_{42}$  taken together form a nitrogen protecting group; or  $R_{41}$  and  $R_{42}$  taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

q is from zero to about 50, provided that when said compound has formula ID, q is at least 1;

M is an optionally protected internucleoside linkage;

(b) reacting said compound of formula I with a compound of formula II:

$$R_{30}$$
—NH $-X_3$ -C—OH

II

wherein:

R<sub>30</sub> is an amino protecting group;

X<sub>3</sub> is a group of formula XII:

XII

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wherein m is 1 or 2;

R<sub>4</sub> is a hydroxyl group, or a protected hydroxyl group; to form a compound of formula IVA, IVB, IVC, or IVD:

$$R_{1} = O$$

$$R_{21}$$

$$R_{20}$$

$$R_{20}$$

$$R_{21}$$

$$R_{21}$$

$$R_{21}$$

$$R_{21}$$

$$R_{21}$$

$$R_1$$
-O  $O$   $B$   $R_{21}$   $q$   $O$   $B$   $W_4$   $R_{21}$   $IV B$ 

$$W = \begin{bmatrix} 0 & B \\ R_{21} & q \\ R_{20} & R_{21} \end{bmatrix}$$
IV C

IVD

wherein:

W<sub>4</sub> has the formula:

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where W<sub>1</sub> is a linking group, O, NH, or S; and treating said compound of formula IVA, IVB, IVC or IVD with a deprotecting reagent to form a compound of formula VA, VB, VC or VD:

$$R_{1} = O \longrightarrow B$$

$$R_{21} \longrightarrow Q$$

$$R_{20} \longrightarrow W_{5}$$

$$VA$$

$$VB$$

$$R_{1} = O \longrightarrow B$$

$$R_{21} \longrightarrow Q$$

$$R_{21} \longrightarrow Q$$

$$R_{21} \longrightarrow Q$$

$$R_{20} \longrightarrow R_{21}$$

wherein W<sub>5</sub> has the formula:

V D

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$$O \longrightarrow N \longrightarrow NH$$

$$R_5 \longrightarrow N \longrightarrow NH$$

$$R_6$$

condensing said compound of Formula V with a compound of Formula VI:

VI

wherein:

R<sub>5</sub> is H or an amino protecting group;

R<sub>6</sub> is H or an amino protecting group;

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to form a compound of Formula VIIA, VIIB, VIIC, or VIID:

VIIA

$$R_1$$
—O  $M$ 
 $W_7$ 
 $Q$ 
 $R_{20}$ 
 $R_{21}$ 
VIID

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wherein W<sub>7</sub> has the Formula:

(d) contacting said compound of Formula VIIA or VIID with a phosphitylating reagent to form a compound of Formula VIIIA or VIIID:

$$R_1$$
-O  $B$ 
 $R_1$ -O  $B$ 
 $R_2$ 1

 $R_3$ -O  $R_2$ 1

 $R_3$ -O  $R_2$ 1

 $R_3$ -O  $R_2$ 1

 $R_3$ -O  $R_2$ 1

VIIIA

VIIID

wherein W<sub>7</sub> has the Formula:

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$$\{-w_1-C-x_3-NH \bigcup_{O} \bigvee_{R_5} \bigvee_{N} \bigvee_{NH} \bigvee_{NH} R_6$$

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106 (Currently Amended).

A synthetic method comprising the steps of:

providing a compound of formula IA, IB, IC or ID: (a)

$$\begin{array}{c|c} W_1 a & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ &$$

ID

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## wherein:

W<sub>1a</sub> is W<sub>1b</sub>-H, OH, NH<sub>2</sub> or SH, where W<sub>1b</sub> is a linking group;

R<sub>1</sub> is H or a hydroxyl protecting group;

B is a nucleobase;

each R<sub>21</sub> is H, OH, F, or a group of formula Z-R<sub>22</sub>-(R<sub>23</sub>)<sub>v</sub>;

Z is O, S, NH, or N- $R_{22}$ - $(R_{23})_v$ 

 $R_{22}$  is  $C_1$ - $C_{20}$  alkyl,  $C_2$ - $C_{20}$  alkenyl, or  $C_2$ - $C_{20}$  alkynyl;

R<sub>23</sub> is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether, a group that enhances the pharmacodynamic properties of oligonucleotides, or a group that enhances the pharmacokinetic properties of oligonucleotides;

v is from 0 to about 10;

or  $R_{21}$  has one of the formulas:

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$$\boxed{ (O)_{y1} - (CH_2)_{y2} } O - E$$

$$---(O)_{y1}--(CH_{2})_{y2}--O-N-(CH_{2})_{y2}-O-E$$

wherein:

y1 is 0 or 1; y2 is 0 to 10; y3 is 1 to 10;

E is  $N(R_{41})(R_{42})$  or  $N=C(R_{41})(R_{42})$ ;

each  $R_{41}$  and each  $R_{42}$  is independently H,  $C_1$ - $C_{10}$  alkyl, a nitrogen protecting group, or  $R_{41}$  and  $R_{42}$  taken together form a nitrogen protecting group; or  $R_{41}$  and  $R_{42}$  taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

q is from zero to about 50, provided that when said compound has formula ID, q is at least 1;

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M is an optionally protected internucleoside linkage;

reacting said compound of formula I with a compound of formula II: (b)

$$R_{30}$$
—NH $-X_3$ -C—OH

II

wherein:

R<sub>30</sub> is an amino protecting group;

X<sub>3</sub> is a group of formula XI:

$$\left\{ -(CH_2)_{p} \right\}$$

XI

wherein:

p is 1 or 2;

R<sub>4</sub> is a hydroxyl group, or a protected hydroxy group;

or  $X_3$  is a group of formula XII:

$$\{$$
  $\}_{m}$ 

XII

wherein m is 1 or 2;

 $Z_1$  is the sidechain of a naturally occurring amino acid, or a protected sidechain of a naturally occurring amino acid;

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R<sub>4</sub> is a hydroxyl group, or a protected hydroxyl group;

p is 1 or 2; to form a compound of formula IVA, IVB, IVC, or IVD:

$$R_1$$
—O  $B$ 
 $W_4$ 
 $Q$ 
 $R_{20}$ 
 $R_{21}$ 

IVD

wherein:

W<sub>4</sub> has the formula:

IVC

$$\left\{ -W_{1} - C - X_{3} - N - R_{30} \right\}$$

where W<sub>1</sub> is a linking group, O, NH, or S; and

V D

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treating said compound of formula IVA, IVB, IVC or IVD with a deprotecting reagent to form a compound of formula VA, VB, VC or VD:

$$R_{1} = 0$$

$$R_{21} = 0$$

$$R$$

wherein  $W_5$  has the formula:

VC

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(c) condensing said compound of Formula V with a compound of Formula VI:

$$O \longrightarrow N \longrightarrow NH$$

$$R_5 \longrightarrow N \longrightarrow NH$$

$$R_6$$

VI

wherein:

R<sub>5</sub> is H or an amino protecting group;

R<sub>6</sub> is H or an amino protecting group;

to form a compound of Formula VIIA, VIIB, VIIC, or VIID:

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$$\begin{array}{c|c} W_7 & & & \\ & & & \\ & & & \\ M & & & \\ & & & \\ R_{20} & R_{21} \end{array}$$

VIIC

$$R_1$$
-O  $B$ 
 $R_{21}$ 
 $q$ 
 $W_7$ 
 $R_{21}$ 

VIID

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wherein W<sub>7</sub> has the Formula:

wherein said compound of formula VI is prepared by the steps of reacting a compound of formula IX:

with a compound of formula X:

$$H_2N$$
 $C$ 
 $C$ 
 $C$ 
 $C$ 
 $C$ 

and treating the product of said reaction with a protecting group reagent to form said compound of formula VI.

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Claims 107-109 (Canceled)

110 (New). The compound of claim 112 wherein said  $R_{20}$  is a group of formula:

$$R_3$$
— $O$ 
 $R_2$ 

wherein  $R_2$  is diisopropylamino and  $R_3$  is  $\beta$ -cyanoethyl.

111 (New). The compound of claim 67 wherein  $R_{20}$  is a group of formula:

where  $R_3$  is  $\beta$ -cyanoethyl, and  $R_2$  is diisopropylamino.

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112 (New). A compound having formula XVIA, XVIB, XVIC or XVID:

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wherein:

W<sub>14</sub> has the formula

$$-X_{6}-X_{5}-X_{4}-N \longrightarrow R_{5}" \longrightarrow N \longrightarrow N \longrightarrow R_{6}$$

wherein:

 $X_4$  is -CH( $X_4$ ) or a group of formula:

$$-(CH_2)_t$$

 $X_{4'}$  is the side chain of a naturally-occurring or non-naturally-occurring amino acid, or a protected side chain of a naturally-occurring or non-naturally-occurring amino acid;

t is 1 or 2;

 $X_5$  is -N( $X_6$ )C(O)-, -C(O)NH-, -NHC(O)-, -OC(O)NH-,-C(S)NH-, -SC(S)NH-, -SC(O)NH-, -OC(S)NH-, -C(O)O-, -C(O)(CH<sub>2</sub>)<sub>n</sub>- or a bond;

n is an integer from 1 to 50;

each  $X_6$  and  $X_{6'}$  is, independently, a bond, hydrogen or a hydrocarbyl group selected from  $C_1$ - $C_{10}$  alkyl,  $C_2$ - $C_{10}$  alkenyl,  $C_2$ - $C_{20}$  alkynyl,  $C_6$ - $C_{14}$  aryl,  $C_6$ - $C_{14}$  aralkyl,  $C_3$ - $C_{14}$  cycloalkyl,  $C_5$ - $C_{14}$  fused cycloalkyl,  $C_4$ - $C_{14}$  heterocycle,  $C_4$ - $C_{14}$  heterocyclylalkyl,  $C_4$ - $C_{14}$  heteroarylalkyl; wherein said hydrocarbyl group is substituted with at least two hydroxyl groups,

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and is optionally substituted with oxo, acyl, alkoxy, alkoxycarbonyl, alkyl, alkenyl, alkynyl, amino, amido, azido, aryl, heteroaryl, carboxylic acid, cyano, guanidino, halo, haloalkyl, haloalkoxy, hydrazino, ODMT, alkylsulfonyl, nitro, sulfide, disulfide, sulfone, sulfonate, sulfonamide, thiol, and thioalkoxy; provided that  $X_6$  is not hydrogen and  $X_6$  is not a bond;

R<sub>1</sub> is hydrogen or a hydroxyl protecting group;

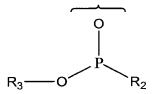
R<sub>4</sub> is a hydroxyl group or a protected hydroxyl group;

each  $R_{5'}$  and  $R_{40}$  is, independently, hydrogen,  $C_1$ - $C_{10}$  alkyl,  $C_2$ - $C_{10}$  alkenyl,  $C_2$ - $C_{20}$  alkynyl,  $C_6$ - $C_{14}$  aryl or an amino-protecting group

 $R_{5"}$  is hydrogen,  $C_1$ - $C_{10}$  alkyl,  $C_2$ - $C_{10}$  alkenyl,  $C_2$ - $C_{20}$  alkynyl,  $C_6$ - $C_{14}$  aryl,  $C_6$ - $C_{14}$  aralkyl,  $C_3$ - $C_{14}$  cycloalkyl, formyl, aminoalkyl or hydroxymethyl;

R<sub>6</sub> is hydrogen or an amino protecting group;

R<sub>20</sub> is hydroxyl or a group of formula:



 $R_2$  is  $-N(R_7)_2$ , or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

R<sub>7</sub> is straight or branched chain alkyl having from 1 to 10 carbons;

R<sub>3</sub> is a phosphorus protecting group;

 $R_{21}$  is hydrogen, hydroxyl, fluoro or a group of formula  $Z-R_{22}-(R_{23})_v$ ;

Z is O, S, NH or  $N-R_{22}-(R_{23})_v$ ;

 $R_{22}$  is  $C_1$ - $C_{20}$  alkyl,  $C_2$ - $C_{20}$  alkenyl, or  $C_2$ - $C_{20}$  alkynyl;

R<sub>23</sub> is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-

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aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether;

or R<sub>21</sub> has one of the formulas:

$$(O)_{y_1}$$
  $- (CH_2)_{y_2}$   $O$   $- E$ 

$$---(O)_{y_1} - ---(CH_2)_{y_2} - O - N - ----(CH_2)_{y_2} - O - E$$

wherein:

y1 is 0 or 1; each y2 is, independently, 0 to 10; y3 is 1 to 10; E is N(R<sub>41</sub>)(R<sub>42</sub>) or N=C(R<sub>41</sub>)(R<sub>42</sub>);

each  $R_{41}$  and each  $R_{42}$  is independently H,  $C_1$ - $C_{10}$  alkyl, a nitrogen protecting group, or  $R_{41}$  and  $R_{42}$  taken together form a nitrogen protecting group; or  $R_{41}$  and  $R_{42}$  taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

B is a nucleobase;

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M is an optionally protected internucleoside linkage;

q is 0 to about 50; and

v is from zero to about 10;

provided that when said compound has formula XVID, q is at least 1.

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113 (New). A compound having formula XVIA, XVIB, XVIC or XVID:

$$W_{14}$$
 $O$ 
 $B$ 
 $M$ 
 $R_{21}$ 
 $Q$ 
 $B$ 
 $Q$ 
 $B$ 
 $Q$ 
 $R_{20}$ 
 $R_{21}$ 

XVIC

**XVIB** 

$$\begin{array}{c} R_1O & \\ \\ M & W_{14} \end{array} \begin{array}{c} \\ \\ \\ R_{20} & R_{21} \end{array}$$
 XVID

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wherein:

W<sub>14</sub> has the formula:

$$-X_{6}-X_{5}-X_{4}-N$$
 $X_{9}$ 
 $X_{9}$ 
 $X_{1}$ 
 $X_{1}$ 
 $X_{1}$ 
 $X_{1}$ 
 $X_{2}$ 
 $X_{3}$ 
 $X_{4}$ 
 $X_{5}$ 
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 $X_{5}$ 
 $X_{1}$ 
 $X_{1}$ 
 $X_{2}$ 
 $X_{3}$ 
 $X_{4}$ 
 $X_{5}$ 
 $X_{5}$ 

wherein:

 $X_4$  is -CH( $X_4$ ) or a group of formula:

$$-(CH_2)_t$$

 $X_{4'}$  is the side chain of a naturally-occurring or non-naturally-occurring amino acid, or a protected side chain of a naturally-occurring or non-naturally-occurring amino acid;

t is 1 or 2;

 $X_5 \text{ is -N(X}_6)C(O)-, -C(O)NH-, -NHC(O)-, -OC(O)NH-, -C(S)NH-, -SC(S)NH-, -SC(O)NH-, -OC(S)NH-, -C(O)O-, -C(O)(CH_2)_n- or a bond;$ 

n is an integer from 1 to 50;

each  $X_6$ ,  $X_6$  and  $X_9$  is, independently, a bond, hydrogen or a hydrocarbyl group selected from  $C_1$ - $C_{10}$  alkyl,  $C_2$ - $C_{10}$  alkenyl,  $C_2$ - $C_{20}$  alkynyl,  $C_6$ - $C_{14}$  aryl,  $C_6$ - $C_{14}$  aralkyl,  $C_3$ - $C_{14}$  cycloalkyl,

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 $C_5$ - $C_{14}$  fused cycloalkyl,  $C_4$ - $C_{14}$  heterocycle,  $C_4$ - $C_{14}$  heterocyclylalkyl,  $C_4$ - $C_{14}$  heteroaryl and  $C_4$ - $C_{14}$  heteroarylalkyl; wherein said hydrocarbyl group is substituted with at least two hydroxyl groups, and is optionally substituted with oxo, acyl, alkoxy, alkoxycarbonyl, alkyl, alkenyl, alkynyl, amino, amido, azido, aryl, heteroaryl, carboxylic acid, cyano, guanidino, halo, haloalkyl, haloalkoxy, hydrazino, ODMT, alkylsulfonyl, nitro, sulfide, disulfide, sulfone, sulfonate, sulfonamide, thiol, and thioalkoxy; provided that each  $X_6$  and  $X_9$  is not hydrogen and  $X_6$  is not a bond;

 $R_1$  is hydrogen or a hydroxyl protecting group;

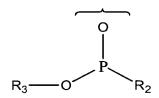
R<sub>4</sub> is a hydroxyl group or a protected hydroxyl group;

each  $R_{5'}$  and  $R_{40}$  is, independently, hydrogen,  $C_1$ - $C_{10}$  alkyl,  $C_2$ - $C_{10}$  alkenyl,  $C_2$ - $C_{20}$  alkynyl,  $C_6$ - $C_{14}$  aryl or an amino-protecting group

 $R_{5"}$  is hydrogen,  $C_1$ - $C_{10}$  alkyl,  $C_2$ - $C_{10}$  alkenyl,  $C_2$ - $C_{20}$  alkynyl,  $C_6$ - $C_{14}$  aryl,  $C_6$ - $C_{14}$  aralkyl,  $C_3$ - $C_{14}$  cycloalkyl, formyl, aminoalkyl or hydroxymethyl;

R<sub>6</sub> is hydrogen or an amino protecting group;

R<sub>20</sub> is hydroxyl or a group of formula:



 $R_2$  is  $-N(R_7)_2$ , or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

R<sub>7</sub> is straight or branched chain alkyl having from 1 to 10 carbons;

R<sub>3</sub> is a phosphorus protecting group;

 $R_{21}$  is hydrogen, hydroxyl, fluoro or a group of formula Z- $R_{22}$ - $(R_{23})_v$ ;

Z is O, S, NH or N- $R_{22}$ - $(R_{23})_v$ ;

 $R_{22}$  is  $C_1\text{-}C_{20}$  alkyl,  $C_2\text{-}C_{20}$  alkenyl, or  $C_2\text{-}C_{20}$  alkynyl;

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R<sub>23</sub> is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether;

or  $R_{21}$  has one of the formulas:

$$---(O)_{y1} - ---(CH_2)_{y2} - O - N - ----(CH_2)_{y2} - O - E$$

wherein:

y1 is 0 or 1; each y2 is, independently, 0 to 10; y3 is 1 to 10; E is  $N(R_{41})(R_{42})$  or  $N=C(R_{41})(R_{42})$ ;

each  $R_{41}$  and each  $R_{42}$  is independently H,  $C_1$ - $C_{10}$  alkyl, a nitrogen protecting group, or  $R_{41}$  and  $R_{42}$  taken together form a nitrogen protecting group; or  $R_{41}$  and  $R_{42}$  taken together with the N

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or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

B is a nucleobase;

M is an optionally protected internucleoside linkage;

q is 0 to about 50; and

v is from zero to about 10;

provided that when said compound has formula XVIC, at least one  $R_{21}$  is a group other than hydrogen, and when said compound has formula XVIC or XVID, q is at least 1.

114 (New) A compound having formula XVIA, XVIB, XVIC or XVID:

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$$W_{14} = \begin{cases} & & & \\ & &$$

$$\begin{array}{c|c} R_1O & B \\ \hline M & W_{14} \\ \hline Q & B \\ \hline R_{20} & R_{21} \\ \hline XVID \end{array}$$

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wherein:

W<sub>14</sub> has the formula:

wherein:

 $X_4$  is -CH( $X_4$ ) or a group of formula:

$$-(CH_2)_t$$

 $X_{4'}$  is the side chain of a naturally-occurring or non-naturally-occurring amino acid, or a protected side chain of a naturally-occurring or non-naturally-occurring amino acid;

t is 1 or 2;

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 $X_5$  is -N( $X_6$ )C(O)-, -C(O)NH-, -NHC(O)-, -OC(O)NH-, -C(S)NH-, -SC(S)NH-, -SC(O)NH-, -OC(S)NH-, -C(O)O-, -C(O)(CH<sub>2</sub>)<sub>n</sub>- or a bond;

n is an integer from 1 to 50;

each  $X_6$  and  $X_6$  is, independently, a bond, hydrogen or a hydrocarbyl group selected from  $C_1$ - $C_{10}$  alkyl,  $C_2$ - $C_{10}$  alkenyl,  $C_2$ - $C_{20}$  alkynyl,  $C_6$ - $C_{14}$  aryl,  $C_6$ - $C_{14}$  aralkyl,  $C_3$ - $C_{14}$  cycloalkyl,  $C_5$ - $C_{14}$  fused cycloalkyl,  $C_4$ - $C_{14}$  heterocycle,  $C_4$ - $C_{14}$  heterocyclylalkyl,  $C_4$ - $C_{14}$  heteroaryl and  $C_4$ - $C_{14}$  heteroarylalkyl; wherein said hydrocarbyl group is substituted with at least two hydroxyl groups, and is optionally substituted with oxo, acyl, alkoxy, alkoxycarbonyl, alkyl, alkenyl, alkynyl, amino, amido, azido, aryl, heteroaryl, carboxylic acid, cyano, guanidino, halo, haloalkyl, haloalkoxy, hydrazino, ODMT, alkylsulfonyl, nitro, sulfide, disulfide, sulfone, sulfonate, sulfonamide, thiol, and thioalkoxy; provided that  $X_6$  is not hydrogen and  $X_6$  is not a bond;

R<sub>1</sub> is hydrogen or a hydroxyl protecting group;

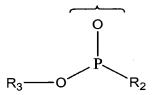
R<sub>4</sub> is a hydroxyl group or a protected hydroxyl group;

each  $R_{5'}$  and  $R_{40}$  is, independently, hydrogen,  $C_1$ - $C_{10}$  alkyl,  $C_2$ - $C_{10}$  alkenyl,  $C_2$ - $C_{20}$  alkynyl,  $C_6$ - $C_{14}$  aryl or an amino-protecting group

 $R_{5"}$  is hydrogen,  $C_1$ - $C_{10}$  alkyl,  $C_2$ - $C_{10}$  alkenyl,  $C_2$ - $C_{20}$  alkynyl,  $C_6$ - $C_{14}$  aryl,  $C_6$ - $C_{14}$  aralkyl,  $C_3$ - $C_{14}$  cycloalkyl, formyl, aminoalkyl or hydroxymethyl;

R<sub>6</sub> is hydrogen or an amino protecting group;

 $R_{20}$  is hydroxyl or a group of formula:



 $R_2$  is  $-N(R_7)_2$ , or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

R<sub>7</sub> is straight or branched chain alkyl having from 1 to 10 carbons;

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R<sub>3</sub> is a phosphorus protecting group;

R<sub>21</sub> is hydrogen, hydroxyl, fluoro or a group of formula Z-R<sub>22</sub>-(R<sub>23</sub>)<sub>v</sub>;

Z is O, S, NH or N- $R_{22}$ - $(R_{23})_v$ ;

 $R_{22}$  is  $C_1$ - $C_{20}$  alkyl,  $C_2$ - $C_{20}$  alkenyl, or  $C_2$ - $C_{20}$  alkynyl;

R<sub>23</sub> is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether;

or  $R_{21}$  has one of the formulas:

$$--(O)_{y1}$$
  $--(CH_2)_{y2}$   $--O$   $N$   $--(CH_2)_{y2}$   $--O$   $--E$ 

wherein:

y1 is 0 or 1; each y2 is, independently, 0 to 10; y3 is 1 to 10; E is  $N(R_{41})(R_{42})$  or  $N=C(R_{41})(R_{42})$ ; DOCKET NO.: ISIS-4803
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each  $R_{41}$  and each  $R_{42}$  is independently H,  $C_1$ - $C_{10}$  alkyl, a nitrogen protecting group, or  $R_{41}$  and  $R_{42}$  taken together form a nitrogen protecting group; or  $R_{41}$  and  $R_{42}$  taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

B is a nucleobase;

M is an optionally protected internucleoside linkage;

q is 0 to about 50; and

v is from zero to about 10;

provided that when said compound has formula XVID, q is at least 1.

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## 115 (New) A compound having the formula XIIIA, XIIIB, XIIIC or XIIID:

$$R_1$$
 O B  $R_{21}$   $q$  O B  $R_{20}$   $W_{13}$   $X$  IIIA

$$\begin{array}{c|c} W_{13} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ & & \\ &$$

R<sub>20</sub>

XIIID

wherein:

W<sub>13</sub> has the formula:

$$\{-W_1-C-X_3-NH \}$$

XIIIC

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R<sub>1</sub> is H or a hydroxyl protecting group;

B is a nucleobase;

each R<sub>21</sub> is H, OH, F, or a group of formula Z-R<sub>22</sub>-(R<sub>23</sub>)<sub>v</sub>;

Z is O, S, NH or  $N-R_{22}-(R_{23})_v$ ;

 $R_{22}$  is  $C_1$ - $C_{20}$  alkyl,  $C_2$ - $C_{20}$  alkenyl, or  $C_2$ - $C_{20}$  alkynyl;

R<sub>23</sub> is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether;

or R<sub>21</sub> has one of the formulas:

$$-(O)_{y1}-(CH_2)_{y2}$$
 $-(CH_2)_{y3}$  $-(CH_2)_{y3}$ 

$$---(O)_{y_1} - ---(CH_2)_{y_2} - O - N - ----(CH_2)_{y_2} - O - E$$

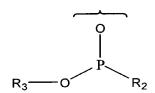
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wherein:

y1 is 0 or 1; y2 is 0 to 10; y3 is 1 to 10; E is N(R<sub>41</sub>)(R<sub>42</sub>) or N=C(R<sub>41</sub>)(R<sub>42</sub>);

each  $R_{41}$  and each  $R_{42}$  is independently H,  $C_1$ - $C_{10}$  alkyl, a nitrogen protecting group, or  $R_{41}$  and  $R_{42}$  taken together form a nitrogen protecting group; or  $R_{41}$  and  $R_{42}$  taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

v is from 0 to about 10;
q is 0 to about 50; and
v is from zero to about 10;
M is an optionally protected internucleoside linkage;
W<sub>1</sub> is a linking group, O, NH or S;
R<sub>20</sub> is hydroxyl or a group of Formula:



 $R_2$  is  $-N(R_7)_2$ , or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

 $R_7$  is straight or branched chain alkyl having from 1 to 10 carbons;

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R<sub>3</sub> is a phosphorus protecting group;

R<sub>5</sub> is H or an amino protecting group;

R<sub>6</sub> is H or an amino protecting group;

 $X_3$  has the formula XII:

$$\left\{\begin{array}{c} \left\{\begin{array}{c} \left\{\right\} \\ \left\{\right\} \\ R_4 \end{array}\right\}$$

XII

wherein m is 1 or 2; and

 $R_4$  is a hydroxyl group, or a protected hydroxyl group; provided that when said compound has formula XIIIC, at least one  $R_{21}$  is a group other than hydrogen, and when said compound has formula XIIIC or XIIID, q is at least 1.

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116 (New) A compound having the formula XVIA, XVIB, XVIC or XVID:

XVIC

$$R_1$$
— $O$ — $O$ — $B$ — $W_{16}$   $q$ 
 $O$ — $B$ 
 $R_{20}$   $R_{21}$ 

XVIB

XVID

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wherein:

W<sub>16</sub> has the formula:

 $R_1$  is H or a hydroxyl protecting group;

B is a nucleobase;

each R<sub>21</sub> is H, OH, F, or a group of formula Z-R<sub>22</sub>-(R<sub>23</sub>)<sub>v</sub>;

Z is O, S, NH or N- $R_{22}$ - $(R_{23})_v$ ;

 $R_{22} \ is \ C_1\text{-}C_{20} \ alkyl, \ C_2\text{-}C_{20} \ alkenyl, \ C_2\text{-}C_{20} \ alkynyl, \ C_1\text{-}C_{20} \ akoxy, \ C_2\text{-}C_{20}$  alkenyloxy, or  $C_2\text{-}C_{20}$  alkynyloxy;

R<sub>23</sub> is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether;

or  $R_{21}$  has one of the formulas:

$$-[(O)_{y1}-(CH_2)_{y2}]_{y3}O-E$$

wherein:

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y1 is 0 or 1;

y2 is 0 to 10; y3 is 1 to 10;

E is  $N(R_{41})(R_{42})$  or  $N=C(R_{41})(R_{42})$ ;

each  $R_{41}$  and each  $R_{42}$  is independently H,  $C_1$ - $C_{10}$  alkyl, a nitrogen protecting group, or  $R_{41}$  and  $R_{42}$  taken together form a nitrogen protecting group; or  $R_{41}$  and  $R_{42}$  taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

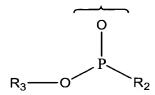
v is from 0 to about 10;

q is 0 to about 50;

M is an optionally protected internucleoside linkage;

W<sub>1</sub> is a linking group;

R<sub>20</sub> is hydroxyl or a group of Formula:



 $R_2$  is  $-N(R_7)_2$ , or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

 $R_7$  is straight or branched chain alkyl having from 1 to 10 carbons;

R<sub>3</sub> is a phosphorus protecting group;

X<sub>3</sub> has the formula XII:

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$$\left\{ \begin{array}{c} \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \end{array} \right\}_{m}$$

XII

wherein m is 1 or 2;

 $R_4$  is a hydroxyl group, or a protected hydroxyl group; and provided that when said compound has formula XVID, q is at least 1.

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117 (New) A compound having the formula XVIIA, XVIIB, XVIIC or XVIID:

**XVIIB** 

XVIIC

$$R_1$$
—O  $B$ 
 $W_{17}$ 
 $q$ 
 $R_{20}$ 
 $R_{21}$ 

XVIID

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wherein:

W<sub>17</sub> has the formula:

$$\{-W_1-C-X_3-NH\bigcup_{\substack{0\\ \\ 0}} NH$$

R<sub>1</sub> is H or a hydroxyl protecting group;

B is a nucleobase;

each R<sub>21</sub> is H, OH, F, or a group of formula Z-R<sub>22</sub>-(R<sub>23</sub>)<sub>v</sub>;

Z is O, S, NH or N- $R_{22}$ - $(R_{23})_v$ ;

 $R_{22}$  is  $C_1$ - $C_{20}$  alkyl,  $C_2$ - $C_{20}$  alkenyl, or  $C_2$ - $C_{20}$  alkynyl;

R<sub>23</sub> is hydrogen, amino, halogen, hydroxyl, thiol, keto, carboxyl, nitro, nitroso, nitrile, trifluoromethyl, trifluoromethoxy, O-alkyl, S-alkyl, NH-alkyl, N-dialkyl, O-aryl, S-aryl, NH-aryl, O-aralkyl, S-aralkyl, NH-aralkyl, amino, N-phthalimido, imidazole, azido, hydrazino, hydroxylamino, isocyanato, sulfoxide, sulfone, sulfide, disulfide, silyl, aryl, heterocycle, carbocycle, intercalator, reporter molecule, conjugate, polyamine, polyamide, polyalkylene glycol, polyether;

or  $R_{21}$  has one of the formulas:

$$-[(O)_{y_1}-(CH_2)_{y_2}]_{y_3}O-E$$

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wherein:

y1 is 0 or 1;

y2 is 0 to 10;

y3 is 1 to 10;

E is  $N(R_{41})(R_{42})$  or  $N=C(R_{41})(R_{42})$ ;

each  $R_{41}$  and each  $R_{42}$  is independently H,  $C_1$ - $C_{10}$  alkyl, a nitrogen protecting group, or  $R_{41}$  and  $R_{42}$  taken together form a nitrogen protecting group; or  $R_{41}$  and  $R_{42}$  taken together with the N or C atom to which they are attached form a ring structure that can include at least one heteroatom selected from N and O;

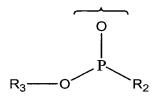
v is from 0 to about 10;

q is 0 to about 50;

M is an optionally protected internucleoside linkage;

W<sub>1</sub> is a linking group, O, NH or S;

 $R_{20}$  is hydroxyl or a group of Formula:



 $R_2$  is  $-N(R_7)_2$ , or a heterocycloalkyl or heterocycloalkenyl ring containing from 4 to 7 atoms, and having up to 3 heteroatoms selected from nitrogen, sulfur, and oxygen;

R<sub>7</sub> is straight or branched chain alkyl having from 1 to 10 carbons;

 $R_3$  is a phosphorus protecting group;

 $X_3$  has the formula XII:

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XII

wherein m is 1 or 2;

 $R_4$  is a hydroxyl group, or a protected hydroxyl group; and

R<sub>5</sub> is H or an amino protecting group;

provided that when said compound has formula XVIID, q is at least 1.